

PATENT COOPERATION TREATY

CR
3)

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

REITSTÖTTER-KINZEBACH & PARTNER
(GbR)
Sternwartstrasse 4
81679 München
ALLEMAGNE

Patentanwälte
Reitstötter, Kinzebach & Part.
Eing. 21. März 2005
Sternwartstr. 4 D-81679 München

18.03.05
PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year)

17.03.2005

Applicant's or agent's file reference
M/43348-PCT

IMPORTANT NOTIFICATION

International application No. PCT/EP 03/14422	International filing date (day/month/year) 17.12.2003	Priority date (day/month/year) 18.12.2002
--	--	--

Applicant
FERRER INTERNACIONAL, S.A. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/M/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Pfitzner, G
Tel. +49 89 2399-8032



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M/43348-PCT	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/14422	International filing date (day/month/year) 17.12.2003	Priority date (day/month/year) 18.12.2002	
International Patent Classification (IPC) or both national classification and IPC A61K31/4178			
Applicant FERRER INTERNACIONAL, S.A. et al.			

<ol style="list-style-type: none"> This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. This REPORT consists of a total of 6 sheets, including this cover sheet. <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 4 sheets.</p> This report contains indications relating to the following items: <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the opinion II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 01.07.2004	Date of completion of this report 17.03.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Beeck, M Telephone No. +49 89 2399-8473



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/14422

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-14 as originally filed

Claims, Numbers

1-27 received on 28.02.2005 with letter of 28.02.2005

Drawings, Sheets

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/14422

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,

claims Nos. 26,27

because:

the said international application, or the said claims Nos. 26,27 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the Standard.

the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-27

No: Claims

Inventive step (IS) Yes: Claims 5-17

No: Claims 1-4,18-27

Industrial applicability (IA) Yes: Claims 1-25

No: Claims

2. Citations and explanations

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/14422

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/14422

D1: WO 03/032948 A (MCNEIL-PPC, INC.) 24 April 2003 (2003-04-24)

D2: J. TORRES ET AL: "Sertaconazole in the treatment of mycoses; from dermatology to gynaecology" INTERNATIONAL JOURNAL OF GYNAECOLOGY AND OBSTETRICS, vol. 71, no. S1, December 2000 (2000-12), pages S3-S20, XP002250812 New York (US)

SECTION III:

Claims 26 and 27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

SECTION V:

- 1) The examination has been carried out assuming that the priority is valid, so that P-document D1 has not been taken into consideration.
- 2) The subject-matter of the claims is novel.
- 3) Closest prior art document for the assessment of inventive step is document D2 which already describes the use of 2% sertaconazole for the treatment of vulvovaginal candidiasis (see the abstract and chapters 2 to 5).

The subject-matter of the claims differs therefrom in that the proportion of sertaconazole is higher than 2% and does not exceed 10%.

Hence, the problem to be solved was to provide a composition for the treatment of vaginal candidiasis, using a higher concentration of the active ingredient.

However, the routine experimentation to optimize the required amounts of ingredients of known compositions for a known use falls within the normal capacity of the average skilled person so that *prima facie* the subject-matter of the claims does not involve an inventive step.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/14422

But the figure in conjunction with examples 1 and 2 in the present patent shows the advantageous property of a composition containing 6% sertaconazole.

Therefore the subject-matter of claim 5 involves an inventive step.

4) However, the presence of an inventive step must be shown over the whole range of the concentration of sertaconazole as claimed, which has not been done.

Therefore the subject-matter of claims 1 to 4 and 18 to 27 does not involve an inventive step (Article 33 (3) PCT).

5) In view of the additional differences from the state of the art the subject-matter of claims 6 to 17 involves an inventive step.

6) For the assessment of the present claims 26 and 27 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

CLAIMS

1. A vaginal mucoadhesive composition for single dose administration, which is a cream or a gel and comprises sertaconazole or one of its pharmaceutically acceptable salts wherein the proportion of sertaconazole or the salt is higher than 2 % and does not exceed 10 %.
2. The composition of claim 1, wherein the proportion of sertaconazole or the salt is from 3 to 10 %.
3. The composition of claim 1 or 2, which is a cream.
4. The composition of any one of claims 1 to 3, wherein the pharmaceutically acceptable salt is sertaconazole nitrate.
5. The composition of claim 4, wherein the proportion of sertaconazole nitrate is from 6 to 7 %.
6. The composition of any one of claims 1 to 5, wherein the cream contains lipophilic excipients, mucoadhesive excipients and one or more preservatives, and the gel dosage form contains mucoadhesive excipients and one or more preservatives.
7. The composition of claim 6, wherein the lipophilic excipients are selected from glyceryl stearates and their derivatives, ketostearyl alcohols, polyoxyethylene glycol ethers of n-alcohols, liquid paraffin, lecithin oil, glycerol and the like.

8. The composition of claim 7, wherein the lipophilic excipients are present in a total proportion of from 10 to 40%.

5

9. The composition of claim 8, wherein the lipophilic excipients are present in a total proportion of from 30 to 35%.

10

10. The composition of claim 6, wherein the mucoadhesive excipients are selected from cellulose polymers, gelatin, colloidal anhydrous silica and polyacrylic acid polymers.

15

11. The composition of claim 10, wherein the mucoadhesive excipients are polyacrylic acid polymers.

20

12. The composition of claim 11, wherein the polyacrylic acid polymers form a mixture of polyacrylic acid polymer cross-linked with divinyl glycol and acrylic acid polymer cross-linked with sucrose or pentaerythritol allyl esters.

25

13. The composition of claim 12, wherein the mixture of polyacrylic acid polymer cross-linked with divinyl glycol and acrylic acid polymer cross-linked with sucrose or pentaerythritol allyl esters are present in a proportion of from 0.1 to 3%.

30

14. The composition of claim 13, wherein the mixture of polyacrylic acid polymer cross-linked with divinyl glycol and acrylic acid polymer cross-linked with

sucrose or pentaerythritol allyl esters are present in a proportion of from 1 to 1.5%.

5 15. The composition of claim 6, wherein the preservatives are selected from parabens, benzoic acid, sorbic acid, boric acid and the like.

10 16. The composition of claim 15, wherein the preservatives are present in a total proportion of

15 17. The composition of claim 16, wherein the preservatives are present in a total proportion of from 0.1 to 0.2%.

20 18. The composition of any one of the preceding claims, wherein its content is packed in a single-dose applicator.

25 19. The composition of claim 18, wherein its capacity is from 4 to 6 ml.

30 20. The composition of claim 19, wherein its capacity is 5 ml.

21. A kit comprising the composition according to claims 1-20, and a cream composition for vulvar application containing sertaconazole or one of its pharmaceutically acceptable salts.

22. The kit of claim 21, wherein the pharmaceutically acceptable salt is sertaconazole nitrate.

23. The kit of claim 22, wherein sertaconazole nitrate is present in a proportion of from 1 to 3%.

5 24. The kit of claim 23, wherein sertaconazole nitrate is present in the proportion of 2%.

10 25. Use of the composition according to claims 1 to 20 for the manufacture of a pharmaceutically acceptable dosage form for the treatment of vulvovaginal candidiasis of the vagina.

15 26. A method for treating vulvovaginal candidiasis, wherein the composition of claim 1 is administered into the vagina of a subject in need of such treatment in a single dose.

20 27. The method of claim 26, wherein additionally a composition containing sertaconazole or one of its pharmaceutically acceptable salts is applied to the vulva in single or repeated dose.

PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Patentanwälte
INTERNATIONAL BUREAU & Part.

To:	Eing. 04. März 2004 <i>Ko/EG</i>
Sternwartstr. 4	D-81679 München
REITSTÖTTER-KINZEBACH	
Sternwartstrasse 4	
81679 München	
Germany	

Date of mailing (day/month/year) 26 February 2004 (26.02.2004)	
Applicant's or agent's file reference M/43348-PCT	IMPORTANT NOTIFICATION
International application No. PCT/EP2003/014422	International filing date (day/month/year) 17 December 2003 (17.12.2003)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 18 December 2002 (18.12.2002)
Applicant FERRER INTERNACIONAL, S.A. et al	

1. By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR", in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. (If applicable) The letters "NR" appearing in the right-hand column denote a priority document which, on the date of mailing of this Form, had not yet been received by the International Bureau under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
3. (If applicable) An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b) (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
18 Dec 2002 (18.12.2002)	PCT/EP02/14488	EP	04 Febr 2004 (04.02.2004)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 338.89.75	Authorized officer Jérôme BRASIER Telephone No. (41-22) 338 8394
--	--

From the INTERNATIONAL BUREAU

PCT**NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES**

(PCT Rule 47.1(c), first sentence)

To:

REITSTÖTTER-KINZEBACH Patentanwälte
 Sternwartstrasse 4 Reitstötter, Kinzebach & Part.
 81679 München
 ALLEMAGNE

Eing. 6 - Juli 2004

Sternwartstr. 4 D-81679 München

Date of mailing (day/month/year)
01 July 2004 (01.07.2004)Applicant's or agent's file reference
M/43348-PCT**IMPORTANT NOTICE**International application No.
PCT/EP2003/014422International filing date (day/month/year)
17 December 2003 (17.12.2003)Priority date (day/month/year)
18 December 2002 (18.12.2002)

Applicant

FERRER INTERNACIONAL, S.A. et al

1. Notice is hereby given that the International Bureau has **communicated**, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this notice:

AU, AZ, BY, CH, CN, CO, DZ, EP, HU, JP, KG, KP, KR, MD, MK, MZ, RU, TM, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, BA, BB, BG, BR, BZ, CA, CR, CU, CZ, DE, DK, DM, EA, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MG, MN, MW, MX, NO, NZ, OA, OM, PH, PL, PT, RO, SC, SD, SE, SG, SK, SL, TJ, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this notice is a copy of the international application as published by the International Bureau on 01 July 2004 (01.07.2004) under No. WO 2004/054576

4. TIME LIMITS for filing a demand for international preliminary examination and for entry into the national phase

The applicable time limit for entering the national phase will, subject to what is said in the following paragraph, be **30 MONTHS** from the priority date, not only in respect of any elected Office if a demand for international preliminary examination is filed before the expiration of **19 months** from the priority date, but also in respect of any designated Office, in the absence of filing of such demand, where Article 22(1) as modified with effect from 1 April 2002 applies in respect of that designated Office. For further details, see *PCT Gazette* No. 44/2001 of 1 November 2001, pages 19926, 19932 and 19934, as well as the *PCT Newsletter*, October and November 2001 and February 2002 issues.

In practice, **time limits other than the 30-month time limit** will continue to apply, for various periods of time, in respect of certain designated or elected Offices. For **regular updates on the applicable time limits** (20, 21, 30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

For filing a **demand for international preliminary examination**, see the *PCT Applicant's Guide*, Volume I/A, Chapter IX. Only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

It is the applicant's sole responsibility to monitor all these time limits.

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Authorized officer

Ellen Moyse

Facsimile No.+41 22 740 14 35

Facsimile No.+41 22 338 89 75